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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
STAPLES, MARK	
ART UNIT	**PAPER NUMBER**
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,698	BERLIN, KURT	
	Examiner	Art Unit	
	Mark Staples	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *25-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 October 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of claims 1-24 of Group I in the reply filed on 03/06/2007 is acknowledged.

Claims 25-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 03/06/2007..

Priority

2. It is noted that this application appears to claim subject matter disclosed in prior Application No. 60/370,690, filed on 04/09/2002. A reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which

entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the

information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Information Disclosure Statement

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Oath/Declaration

4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: there is no date of signature of the inventor.

Specification

5. The use of the trademarks REAL-TIME PCR™, LIGHTCYCLER™, TAQMAN™, and QIAGEN™ have been noted in this application. They and any other trademarks should be capitalized wherever they appear and be accompanied by the generic terminology. It is noted that applicant has identified these trademarks with the trademark notation but these trademarks should be capitalized as well.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

6. Claim 1 is objected to because of the following informalities: the phrase "to be analyzed" in line 1 is redundant to the previous phrase "for analyzing" in line 1. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-7 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 2 is rejected as being indefinite as the converting agent is identified as bisulfite but the claim also recites compounds of bisulfite as converting agents. The nature of these compounds is not defined, and it is unclear if they possess the same property for conversion as bisulfite alone, a modified property, or a new property. While the bisulfite anion can be paired with a cation to form a compound, it is unclear whether this is the intended claim language and even so, the rejection would be maintained.

9. Claim 5 is rejected for an improper Markush group in reciting "selected from a group consisting of". The use of the article "a" to mean any, instead of the article "the" to mean one, is confusing and hence unclear, as there should only be one group.

10. The term "hybridizes preferentially" in claim 1 is a relative term which renders the claim indefinite. The term "hybridizes preferentially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The use of the term "hybridizes preferentially" renders the amplifying of claim 1 and dependant claims 2-7 indefinite.

11. The term "similar to peptides" in claim 18 is a relative term which renders the claim indefinite. The term "similar to peptides" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The use of the term "similar to peptides" renders the amplificates of claim 18 indefinite.

12. Claims 12 and 24 contain the trademark/trade names REAL-TIME PCR™, LIGHTCYCLER™, and TAQMAN™. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe real time technique/detecting amplificates and, accordingly, the identification/description is indefinite.

13. Claim 24 is rejected for an improper Markush group in reciting "from the group comprising". The use of the word "comprising", instead of the word "consisting', leaves open and unclear the number of things that can be selected from. It is also noted that the series of assays in the group should be joined by a conjunction.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application

by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

15. Claims 1-5, 7-10, 12-17, 19-22, and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Eads et al. (2000).

Regarding claims 1-3, Eads et al. teach methods for analyzing methylation at one or more CpG positions in a nucleic acid sample (entire reference), comprising:

a. converting unmethylated cytosine bases in the nucleic acid sample by treatment with an agent, bisulfite (see p. i, 2nd column, 1st sentence of last paragraph) ;

b. amplifying one or more nucleic acids of the treated sample in an amplification reaction, wherein at least two oligonucleotide primer pairs are provided for every CpG position to be analyzed, one of which primer pairs hybridizes preferentially in the case where the CpG to treated nucleic acid was methylated in the original sample before conversion, and further wherein the other of which primer pairs hybridizes preferentially in the case where the CpG to treated nucleic acid was unmethylated in the original sample before conversion (Eads et al. teach the use of primers specific to the converted

methylated sequence and specific to the unconverted methylated sequence, see p. ii, 1st column, 1st full sentence);

c. detecting the amplificates formed in the polymerase reaction in a quantifiable manner (see p. iii 3rd sentence under the section *Results* and Figure 2); and

d. determining the degree of methylation in at least one CpG position of the nucleic acid sample (entire reference, especially Figures 2, 3, 4, and 6).

Regarding claims 8, 9, 13, and 16, EADS et al. teach methods for the analysis of the methylation status of one or more CpG dinucleotides within a nucleic acid sample (entire reference), comprising:

a. in the nucleic acid sample, converting cytosine bases that are unmethylated at the 5-position by treatment with a converting agent, bisulfite (see p. i, 2nd column, 1st sentence of last paragraph) ;

b. amplifying one or more nucleic acids of the treated nucleic acid in a polymerase enzyme reaction by means of at least two primer oligonucleotide pairs, wherein one primer pair amplifies a reference sequence and the other primer pairs are methylation specific primers, and further wherein the amplificates formed from each species of primer pairs differ respectively in at least one of length, sequence, and a detectable label selected from a group consisting of fluorescence labels (see top of column 1 on p. iii for amplification of test gene *MLHI* and the reference gene *ACTB* with different primer pairs as given and each specific to each gene labeled with TAMRA™ and FAM™);

c. detecting the amplificates formed from the primer pairs;

d. measuring the amounts of the amplificates formed from each primer pair; and

e. determining the degree of methylation at each analyzed CpG position (for steps c, d, and e see entire reference, especially Figures 2, 3, 4, and 6).

Regarding claims 19-22, EADS et al. teach methods for the analysis of the methylation status of one or more CpG dinucleotides within a nucleic acid sample (entire reference), comprising:

a. converting cytosine bases that are unmethylated at the 5-position by treatment with a converting agent, bisulfite (see p. i, 2nd column, 1st sentence of last paragraph);

b. amplifying one or more nucleic acids of the treated nucleic acid and of one or two reference samples in a polymerase enzyme reaction by means of one or more methylation specific primer oligonucleotide pairs, wherein the amplificates formed from each species of primer pair differ respectively in at least sequence, and have detecable fluorescence labels (Eads et al. teach the use of primers specific to the methylated sequence, see p. ii, 1st column, 1st full sentence; and for primer sequence differences and flruoescnet labels, see top of column 1 on p. iii for amplification of test gene *MLHI* and the reference gene *ACTB* with different primer pairs as given and each specific to each gene labeled with TAMRA™ and FAM™);

c. detecting the amplificates formed from the primer pairs within each sample

d. measuring the amounts of the amplificates formed from each primer pair in each of the samples; and

e. determining the amount of methylation within the treated sequence by determining the amount ofamplificate formed within the treated sample relative to the amount of amplificate formed within the reference sample or samples for each primer pair (for steps c, d, and e see entire reference, especially Figures 2, 3, 4, and 6).

Regarding claim 4, Eads et al. teach amplificates formed from each primer pair differ from those formed by another primer pair in at least sequence (see the section *Methylight primer and probe sequences* on p. ii).

Regarding claim 5, Eads et al. teach wherein the detectable label is selected from a group consisting of fluorescence labels (see the section *Methylight primer and probe sequences* on p. ii for TAMRA™ and FAM™).

Regarding claims 7, 10, 12, and 24, Eads et al. teach wherein detecting the amplificates is carried out by means of real time PCR, TAQMAN® technology (see Abstract).

Regarding claim 13, Eads et al. teach wherein at least three pairs of primers are used in the polymerase reaction, one of which primer pairs is a reference primer pair that amplifies a non-methylated sequence that acts as a reference sequence (see p. ii for the section *Methylight primer and probe sequences* for at least 4 primer pairs including a reference primer pa*ir*).

Regarding claim 14, Eads et al. teach where the reference primer does not contain a CpG dinucleotide and does not contain a TpG dinucleotide (see p. ii for the section *Methylight primer and probe sequences* and the reference primer set for

MYOD1 where neither primer contains G and hence neither contains CpG or TpG dinucleotides).

Regarding claim 15, Eads et al. teach where the primer pairs that do not amplify the reference sequence include one or more of CpG, TpG, and CpA dinucleotides (see p. ii for the section *Methylight primer and probe sequences* and the reference primer set for *MYOD1* where neither primer contains G and hence neither contains CpG or TpG dinucleotides).

Regarding claim 16, Eads et al. teach wherein the amplificate synthesized from each primer pair is compared to the amplificate from the other primers and to the amount of amplificate from the reference primer (see entire reference, especially Figures 2, 3, 4, and 6).

Regarding claim 17, Eads et al. teach wherein determining the degree of methylation is carried out by determining the amount of each amplificate from each primer pair relative to the amount of amplificate formed from the reference primer pair (see entire reference, especially Figures 2, 3, 4, and 6).

16. Claims 1-6 are rejected under 35 U.S.C. 102(e) as being anticipated by Olek et al. (US Patent No. 6,214,556, issued April 10, 2001, filed on September 22, 1999).

Regarding claims 1- 5, Olek et al. (1999) teach methods for analyzing methylation at one or more CpG positions to be analyzed in a nucleic acid sample (entire patent), comprising:

a. converting unmethylated cytosine bases in the nucleic acid sample by treatment with bisulfite to uracil (see Abstract and claim 1);

b. amplifying by a polymerase reaction (see claim 1) one or more nucleic acids of the treated sample in an amplification reaction, wherein at least two oligonucleotide primer pairs are provided for every CpG position to be analyzed, one of which primer pairs hybridizes preferentially in the case where the CpG to treated nucleic acid was methylated in the original sample before conversion, and further wherein the other of which primer pairs hybridizes preferentially in the case where the CpG to treated nucleic acid was unmethylated in the original sample before conversion (see column 17, lines 39-43: "Each oligonucleotide is specific for one CpG position; this means that it either hybridizes only with the target DNA if the CpG position contained in the oligonucleotide is methylated, or only if this position is specifically unmethylated");

c. detecting the amplificates formed in the polymerase reaction in a quantifiable manner including fluorescent labeld PCR products (see column 4, line 39); and

d. determining the degree of methylation in at least one CpG position of the nucleic acid sample.

Regarding claim 6, Olek et al. teach methods of detecting the amplificates by means of mass spectrometry, including MALDI and ESI (see claim 16 and see column 23 lines 31-35).

17. Claims 1-6 are rejected under 35 U.S.C. 102(e) as being anticipated by Olek et al. (WO 2002/002809, filed on 02 July 2001, in English and designating the US).

Regarding claims 1-5, Olek et al. (Jan. 2002) teach methods for ascertaining genetic and/or epigenetic parameters for the diagnosis and/or therapy by analyzing cytosine methylations (entire publication especially claim 16), characterized in that the following steps are carried out:

- in a genomic DNA sample, cytosine bases which are unmethylated at the 5-position are converted, by chemical treatment including bisulfite (see claim 17) to uracil or another base which is dissimilar to cytosine in terms of hybridization behaviour;

- fragments of the chemically pretreated genomic DNA are amplified using sets of primer oligonucleotides (see claim 8 for multiple primers of SEQ ID 1-46 having different sequences) and a polymerase, the amplificates carrying a detectable label which can be fluorescent (see claim 22) and use of primer specific to methylation status (see 2nd paragraph, next last sentence and incorporation by reference of *Nucleic Acids Res.* 1997 Jun 15;25(12):2529-31 and WO 95100669);

- amplificates are hybridized to a set of oligonucleotides andlor PNA probes;

- the hybridized amplificates are subsequently detected.

Regarding claim 6, Olek et al. (Jan. 2002) teach methods of detecting the amplificates by means of mass spectrometry, including MALDI and ESI (see claim 27).

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

19. Claims 11, 18, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eads et al. as applied to claims 1, 10, 18, and 20 above, and further in view of Olek et al. (1999).

Claim 18 is interpreted as encompassing the modification of oligomers which is the substitution of PNA (peptide nucleic acid) nucleotides for naturally occurring nucleotides.

Eads et al. teach as noted above.

Eads et al. do not specifically teach mass spectrometry, either MALDI or ESI, and do not specifically teach PNA oligonucleotides.

Regarding claim 11, and 23, Olek et al. (1999) teach methods of detecting the amplificates by means of mass spectrometry including MALDI and ESI (see claim 16 and see column 23 lines 31-35) including oligonucleotide which are modified by substitutions with PNA nucleotides (see column 17, lines 21-22).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the methods of Eads et al. by using PNA nucleotides and detection by MALDI or ESI as suggested by Olek et al. (1999) with a reasonable expectation of success. The motivation to do so is provided by provided by Olek et al. (1999) who teach: "Furthermore, the scope of protection should also include oligonucleotides used as amplification primers, which are used within the overall concept of the method . . . such as, for example, oligonucleotides based on PNA

(protein-nucleic acid), chemically modified oligonucleotides: and modified or unmodified oligonucleotide . . ." (see column 17 line 15-24) and: "A variant of the method was developed which allows the detection of very large numbers of cytosines and/or guanines in bisulfite-treated DNA by mass spectrometric measurement of lengths in mass spectrometers based on MALDI" (see column 20 lines 58-61). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

20. Claims 11, 18, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eads et al. as applied to claims 1, 10, 18, and 20 above, and further in view of Olek et al. (WO 2002/002809, published 10 January 2002).

Claim 18 is interpreted as encompassing the modification of oligomers which is the substitution of PNA (peptide nucleic acid) nucleotides for naturally occurring nucleotides.

Eads et al. teach as noted above.

Eads et al. do not specifically teach mass spectrometry, either MALDI or ESI, and do not specifically teach PNA oligonucleotides.

Regarding claim 11, and 23, Olek et al. (Jan. 2002) teach methods of detecting the amplificates by means of mass spectrometry, including MALDi or ESI (see claim 27) and oligomers which are modified by substitutions with PNA nucleotides (see Abstract and claim 16).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the methods of Eads et al. by using PNA nucleotides and detection by MALDI or ESI as suggested by Olek et al. (Jan. 2002) with a reasonable expectation of success. The motivation to do so is provided by Olek et al. (Jan. 2002) who teach " . . . PNA-oligomers for detecting the cytosine methylation state of genes . . ." (see Abstract). Further motivation is provided by Olek et al. (Jan. 2002) who teach: "Matrix Assisted Laser Desorption Ionization Mass Spectrometry (MALDI-TOF) is a very efficient development for the analysis of biomolecules" (see p. 5, 1st sentence of 3rd parargraph) and " . . . detection may be carried out and visualized by means of matrix assisted laser desorptionlionization mass spectrometry (MALDI) or using electron spray mass spectrometry (ESI)" (see p. 10, last sentence of 3rd pargraph). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Double Patenting

21. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

22. Claims 1-24 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-35 of copending Application No. 10/493,727. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the copending application are specie methods which use primers to ATC for analysis of methylation status which anticipate the generic methods of the instant application which use primers for analysis of methylation status.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

23. Given the large number of related cases, Applicant is requested to comply with 37 CFR 1.56 by identification of related copending applications and providing a copy of the current version of claims pending in the those applications that are particularly close to issuance, which raise double patenting issues.

Conclusion

24. No claim is free of the prior art.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 7:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark Staples MS
Examiner
Art Unit 1637
May 2, 2007

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
5/3/07